/647 <sub>NT</sub> #4

JAN 1 2002 IN THE U

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**RECEIVED** 

JAN 1 7 2001

TECH CENTER 1600/2900

**Box IDS** 

Assistant Commissioner for Patents Washington, D.C. 20231

### **CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Box IDS, Assistant Commissioner for Patents, Washington, D.C. 20231 on November 7, 2001.

Howard M. Peters (Reg. No. 29,202)

Group Art Unit: 1647

Prior Examiner: Lorraine Spector

#### TRANSMITTAL LETTER

Sir:

Transmitted herewith are the following documents:

- 1. Transmittal Letter (2 pgs.) in duplicate;
- 2. Transmittal of Information Disclosure Statement (2 pgs.) in duplicate; and
- 3. Postcard.

The enclosed are copies of IDS and PTO 1449 forms filed in parent application for the past 12 years. See Serial No. 08/473,276.

If additional fees are due, the Commissioner is hereby authorized to charge such fees or to credit any overpayment to Deposit Account No. 16-1331.

Respectfully submitted,

Date: November 7, 2001

Howard M. Peters (Reg. No. 29,202)

Attorney of Record

PETERS, VERNY, JONES & BIKŠA, LLP

385 Sherman Avenue, Suite 6

Palo Alto, CA 94306

Telephone: (650) 324-1677 Facsimile: (650) 324-1678

Attorney Docket No. 479.58-6 (HMP)

F:\HMP\479.58-6\trn.ltr2.wpd

	F INFORMATION DISCLO Under 37 CFR 1.97(b) or 1.97		Docket No. 479.58-6
In Re Application Of:	NAPOLEONE FERRARA, DENIS	S GOSPODAROWICZ and JE	AN PLOUET
Serial No.	Filing Date	Examiner	Group Art Unit
09/929,770	August 14, 2001	Lorraine Spector	1647
Oud: PERDOTHELIAL	CELL GROWTH FACTOR, ME	THODS OF ISOLATION AND	EXPRESSION
JAN 1 4 2002 (1)			RECEIVED
			JAN 1 7 2001
TRANSAM	Assistant Com	ddress to: nmissioner for Patents yton, D.C. 20231	TECH CENTER 1600/290
•	37 C	FR 1.97(b)	
of a national ap three months of application; befo	Disclosure Statement submitted plication other than a continued the date of entry of the national are the mailing of a first Office Acfiling of a request for continued e	prosecution application under stage as set forth in 37 CFR tion on the merits, or before th	r 37 CFR 1.53(d); within 1.491 in an international e mailing of a first Office
CFR 1.97(b), pr Final Action und	Disclosure Statement submitted ovided that the Information Disc der 37 CFR 1.113, a Notice of sprosecution in the application, a	closure Statement is filed before f Allowance under 37 CFR 1	re the mailing date of a .311, or an Action that
☐ the staten	nent specified in 37 CFR 1.97(e)	;	
	OR		
☐ the fee se	et forth in 37 CFR 1.17(p).		
			·
	·		
·			

142	102 -	<del></del>		
	Selfal No.	Filing Date	Examiner	Group Art Unit
NOOP!	29,770	August 14, 2001	Lorraine Spector	1647
	ENDOTHELIAL	CELL GROWTH FACTOR, ME	THODS OF ISOLATION AND E	EXPRESSION
				RECEIV
				JAN 1 7 2
	· · · · · · · · · · · · · · · · · · ·	Pavr	nent of Fee	TECH CENTER 16
		•	ects to pay the fee set forth in 37 CFR	
a	Certificate of Certify that this docum	ne amount of y overpayment. In y additional fee required.  Fransmission by Facsimile*  ent and authorization to charge deposition to the United States  Office (F )  Signature	Nov. 7, 2001 with as first class mail under addressed to the Assistant Co. Washington, D.C. 20231.	nd fee is being deposited the U.S. Postal Service 37 C.F.R. 1.8 and is ommissioner for Patents,
	Typed or Printed i	Name of Person Signing Certificate	Typed or Printed Name of Po	erson Mailing Certificate
PETEI	(mod)	S & BIKSA, LLP	Dated: November 7, 2001	



U.C. # 89-053-3

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

NAPOLEONE FERRARA, DENIS GOSPODAROWICZ and JEAN PLOUET

Serial No.: 360,235

Filed: June 1, 1989

For: ENDOTHELIAL CELL GROWTH

FACTOR, METHODS OF ISOLA-

TION AND EXPRESSION

Group Art Unit: 186

Examiner: S. Guest

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231

#### CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 on April 30, 1992.

Howard M. Peters (Reg No. 29,202)

# INFORMATION DISCLOSURE STATEMENT SUPPLEMENTAL 37 C.F.R. 1.56 AND 1.97

Sir:

The citations below (copies below), which recently came to the attention of Applicants' attorney, may be material to the examination of the above-identified application and are, therefore, submitted in compliance with the duty of disclosure in 37 C.F.R. 1.56 and 1.97.

A number of these references were published after the filing date of the present or a parent patent application

The Examiner is requested to make these citations of official record in this application.

- 1. G. Beck et al., "Isolation and Characterization of A Vascular Permeability Factor from Stimulated U937 Cells," J. Leukocyte Biol., Vol. 42:5 (1987) p. 568, is an abstract describing the isolation of a vascular permeability factor (VPF) isolated from macrophage cell line U937.
- 2. J. N. Bruce et al., "Vascular permeability induced by protein product of malignant brain tumors: inhibition by dexamethasone," J. Neurosurg., Vol 67 (1987), pp. 880-884 describe an activity caused by a vascular permeability factor (VPF) found in conditioned medium from cultures of malignant human astroglial (brain) tumors. No sequence data are given for the factor.
- 3. G. R. Criscuolo et al., "Further characterization of malignant glioma-derived vascular permeability factor," J. Neurosurg., Vol. 69 (1988), pp. 254-262 describe the VPF referred to in Ref. 2 above. The factor was purified 1000 fold and postulated to have a molecular weight of 42-56 kD. No sequence data is disclosed.
- 4. D. Gospodarowicz et al., "Isolation and characterization of a vascular endothelial cell mitogen produced by pituitary-derived folliculo stellate cells," <a href="Proc. Nat. Acad. Sci.">Proc. Nat. Acad. Sci.</a>, Vol. 86 (1989), pp. 7311-7315, published after the effective filing date of

the present application, describes work done by one of the inventors on the presently claimed FSdGF. An N-terminal sequence of the factor is given.

- 5. J. Plouet et al., "Isolation and characterization of a newly identified endothelial cell mitogen produced by AtT-20 cells," EMBO J., Vol. 8:12 (1989), pp. 3801-3806, published after the effective filing date of the present application describes a human vascular permeability factor, termed hVPF; the N-terminal sequence of HVPF is disclosed. The sequence was found to be similar to the sequence of guinea pig VPF.
- endothelial cell mitogen from a rat glioma-derived cell line,"

  Proc. Nat. Acad. Sci. USA, Vol. 87 (1990), pp. 1323-1327, published after the effective filing date of the present application, describes the purification of a glioma-derived vascular endothelial growth factor (GD-VEFG). An amino acid composition, but not a sequence, is disclosed. The authors state that the disclosed proteins may--or may not--be equivalent to the protein disclosed by Ferrara et al., which is presumptively the presently claimed VEGF.
- 7. G. Conn, "Amino acid and cDNA sequences of a vascular endothelial cell mitogen that is homologous to platelet-derived growth factor," <a href="Proc. Nat. Acad. Sci. USA">Proc. Nat. Acad. Sci. USA</a>, Vol. 87 (1990), pp. 2628-2632, published after the effective filing date of the present application, discloses the complete sequence of the GD-VEGF disclosed in Ref. 6 herein. Homology to platelet derived growth

factor (PDGF) is reported. The paper reports that the sequence of GD-VEGF is 90% similar to a recently reported VEGF sequence, and VEGF sequence (presumably derived from work on the presently claimed protein) is identical to the sequence of VPF.

- 8. D. R. Senger et al., "Purification and NH2-Terminal Amino Acid Sequence of Guinea Pig Tumor-secreted Vascular Permeability Factor," Cancer Res., Vol. 50 (1990), pp. 1774-1778, published after the effective date of the present application, disclose an N-terminal sequence of guinea pig VPF. No similarity between this sequence and previously reported sequences (in the PIR/NBRF sequence database) was found. A note added in the proof cites the work of others relating to VEGF, but no disclosure is made regarding similarity or dissimilarity between VEGF and VPF. The disclosed sequence is not identical to the sequence presently claimed, although visual inspection reveals some similarities between the two sequences.
- 9. N. Ferrara et al., "The Vascular Endothelial Growth Factor Family of Polypeptides," <u>J. Cell. Biochem.</u>, Vol. 47 (1991), pp. 211-218, published after the effective filing date of the present application, is a review of the vascular endothelial growth factors family of polypeptides. The existence of four species of VEGF polypeptides is disclosed.
- 10. C. de Vries et al., "The fms-Like Tyrosine Kinase, a Receptor for Vascular Endothelial Growth Factor," <u>Science</u>, Vol. 255 (1992), pp. 989-991, published after the effective filing date of

479.58-3

<u>PATENT</u> U.C. # 89-053-3

the present application is directed to a receptor for VEGF. An introductory portion of the reference discloses the identity of VPF and VEGF sequences.

This Information Disclosure Statement under 37 C.F.R. and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

If the Examiner has any questions regarding the cited art, she is encouraged to call the undersigned attorney (collect) at (415) 421-2674.

Respectfully submitted,

Howard M. Peters (Reg. No. 29,202)

for

PHILLIPS, MOORE, LEMPIO & FINLEY 177 Post Street, Suite 800 San Francisco, California 94108 Attorneys for Applicant

HMP:cl/kw

Tel: (415) 421-2674 Fax: (415) 421-1663

Enclosures: As listed above

1 P 9.58-3

<u>PATENT</u> U.C. # 89-053-3

JAN 1 4 2002

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of

NAPOLEONE FERRARA, DENIS GOSPODAROWICZ and JEAN PLOUET

Serial No.: 360,235

Filed: June 1, 1989

For: ENDOTHELIAL CELL GROWTH

FACTOR, METHODS OF ISOLA-

TION AND EXPRESSION

Group 180

Group Art Unit: 186

Examiner: S. Guest

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231

#### CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States postal Service as first class mail in an envelope addressed to Commissioner of Patents and Trademarks, Washington, D.C. 20231 on June 18, 1991.

Howard M. Peters (Reg. No. 29,202)

## SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. 1.56 AND 1.97

Sir:

The citations below, copies attached, may be material to the examination of the above-identified application and are, therefore, submitted in compliance with the duty of disclosure in 37 C.F.R. 1.56 and 1.97.

The Examiner is requested to make these citations of official record in this application.

1. D.T. Connolly et al., U.S. Patent 5,008,196, issued April

16, 1991, class 435/240.2.

- California Biotechnology, Inc., International Publ. No.
   WO 91/02058, published 21 February 1991, PCT/US90/04227, filed 27
   July 1990.
- 3. Edmund Tischer et al., "Vascular Endothelial Growth Factor: A New Member of the Platelet-Derived Growth Factor Gen Family," <u>Biochemical & Biophysical Research Communications</u>, Vol. 165 (3), pp. 1198-1206.

This Information Disclosure Statement under 37 C.F.R. and 1.97 is not to be construed as a representation that a search has been made, that additional information material to any examination of this application does not exist, or that anyone or more of these citations constitutes prior act.

If the Examiner has any questions regarding the cited Art, she is encouraged to call the undersigned attorney (collect) at (415) 421-2674.

Respectfully submitted.

Howard M. Peters (Reg. No. 29,202)

for

PHILLIPS, MOORE, LEMPIO & FINLEY 177 Post Street, Ste. 800 San Francisco, CA 94108 Attorneys for Applicants

HMP:cl (415) 421-2674



U.C. # 89-053-3

### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

re the Application of

NAPOLEONE FERRARA, DENIS GOSPODAROWICZ and JEAN PLOUET

Serial No.: 360,235

Filed: June 1, 1989

For: ENDOTHELIAL CELL GROWTH

FACTOR, METHODS OF ISOLA-TION AND EXPRESSION

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231 Group 180

Group Art Unit: 186

Examiner: S. Guest

#### CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States postal Service as first class mail in an envelope addressed to Commissioner of Patents and Trademarks, Washington, D.C. 20231 on October 25, 1990.

Howard M. Peters (Reg. No. 29,202)

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. 1.56 AND 1.97 Sir:

The citations below, copies attached, may be material to the examination of the above-identified application and are, therefore, submitted in compliance with the duty of disclosure in 37 C.F.R. 1.56 and 1.97.

The Examiner is requested to make these citations of official record in this application.

- H.F. Dvorak, et al., U.S. Patent 4,456,550, issued June
   1984, class 260/112R.
- European Patent Application Publication 0370,989,
   published May 30, 1990, class C12N 15/12.
  - H.F. Dvorak, et al. WO 84/02135, PCT, published June 7,

1984, Int. Class C07G 7/00.

- '4. D.W. Leung, et al., "Vascular Endothelial Growth Factor Is a Secreted Angiogenic Mitogen", <u>Science</u>, Vol. 246, p. 1306 (December 8, 1989).
- 5. P.J. Keck, et al., "Vascular Permeability Factor, an Endothelial Cell Mitogen Related to PDGF", <u>Science</u>, Vol. 246, p. 1309, (December 8, 1989).
- 6. G.E. Lemke, et al., "Identification and Purification of Glial Growth Factor<sup>1</sup>", <u>Journal of Neuroscience</u>, Vol. 4, No. 1, p. 75 (January 1984).
- 7. N. Ferrara, et al., "Pituitary Follicular Cells Secrete a Novel Heparin-Binding Growth Factor Specific for Vascular Endothelial Cells", <u>Biochemical and Biophysical Research Communications</u> Vol. 161, No. 2, p. 851, (June 15, 1989).
- 8. D. Gospodarowicz, et al., "Isolation and Characterization of a Vascular Endothelial Cell Mitogen Produced by Pituitary Derived Folliculo Stellate Cells", <u>Biochemistry</u>, Vol. 86 p. 882 (1989).
- 9. D. Gospodarowicz, et al., "Pituitary Follicular Cells Secrete Both Vascular Endothelial Cell Growth Factor and Follistatin" as submitted earlier to related U.S. Patent Application Serial No. 07/346,169 filed May 2, 1990.
- 10. N. Ling, et al., "Isolation and partial characterization of a M<sub>r</sub> 32,000 protein with inhibin activity from porcine follicular fluid", <u>Biochemistry</u>, Vol. 82, p. 7217 (November 1985).
- 11. N. Ueno, et al., "Isolation and partial characterization of follistatin: A single-chain M<sub>r</sub> 35,000 monomeric protein that inhibits the release of follicle-stimulating hormone", Biochemistry, Vol. 84, p. 8282 (December 1987).

If the Examiner has any questions regarding the cited Art, she is encouraged to call the undersigned attorney (collect) at (415)421-2674.

Respectfully submitted,

Howard M. Peters (Reg. No. 29,202)

for PHILLIPS, MOORE, LEMPIO & FINLEY 177 Post Street, Ste. 800 San Francisco, CA 94108 (415) 421-2674 Attorneys for Applicant

HMP: cal A:479-58.3/disclosure

SERIAL NO. TO-1449 (Modified) ATTY, DOCKET NO. 479.58-3 **O/** 360,235 T OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE APPLICANT N. FERRARA et al. **STATEMENT** (Use several sheets if necessary) FILING DATE **GROUP** 186 6/1/89 REFERENCE DESIGNATION **U.S. PATENT DOCUMENTS** EXAMER FILING DATE MILL DOCUMENT NUMBER DATE SUBCLASS NAME auss **F APPROPRIATE** 10 0 8 19 6 4/16/91 Connolly et al 435/240.2 8 AC AD Æ Æ AG AH A FOREIGN PATENT DOCUMENTS TRANSLATION DOCUMENT NUMBER DATE COUNTRY auss SIBCLISS YES published 21/2/91 Patient Cooperation Treaty 2015 8 Ш AN AO R **OTHER** ART (Including Author, Title, Date, Pertinent Pages, Etc.) Edmund Tischer et al., "Vascular Endothelial Growth Factor: A New Member of the Platelet-Derived Growth Factor Gene Family," AR Biochemical & Biophysical Research Communications, Vol. 165(3), pp. 1198-1206. AS ΑT EXAMINER DATE CONSIDERED

EXAMINER: Initial if reference considered, wheth r or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this f rm with n xt communication to applicant.

- `-											<del>,</del>						
			FO	R PTC	)-1449	(Modi	ifi				ATT	Y. DOCKET	NO.		SERIAL NO		
-	LIST	OF P.	ÀTEN	TS A	AND	PUBI	ICA'	TION	S FC	R	479	. 58-3			0, 360,	235	
/	70	Ben	\	STA	TEM	LENT			SURI	E	APPI	ICANT Nap	oleone	Ferrara	a, et al.		
<u> </u>	4 P NAL	È	:/		sheet	s if nec	essary	·)			FILI	NG DATE J	une 1,	1989	GROUP		
RI	NENCE	PDS	NATI(	N		U.S. 1	PATE	NT DO	CUM	ENTS							
E	KAMINER INITIAL				ocu	MENT	NUMI	BER		DATE		NAME		CLASS	SUBCLASS		NG DATI
			4	6	7	0	3	9	4	6/2/87	H.B.	POLLARD	et al	435	240	Nov 1	L6, 19
			4	8	О	1	5	4	1			MURRAY			172.3	Feb 2	
			4	7	3	8	9	2	1			ANIGUCHI			243	Feb	
	-		4	7	8	3.	4	1	1	T		BELL, e		435	240.1		3, 19
_			4	7	2	1	6	7	T			VALLEE,		<del></del>	70	<del></del>	
			-		1			1	1	20/00	, Б. ц.	<u>ر منظمانی ۷۳۹</u>	ec ar	433	70	Jep	20 1.
				<del>                                     </del>	<del> </del>	1								<del></del>	<u> </u>	<del></del>	<del></del>
			<del> </del>		<del>                                     </del>				<del> </del>			<del></del>		<del> </del>			
						-	-										
						-	_	<u> </u>	-								<del></del>
	-	·				-											
							<u> </u>			<u> </u>							
								F	ORE	GN PAT	ENT D	OCUMENT	S		,,,		-
				D.C	actis/	IENT N	NT ISA R	CD		DATE		COLDITA		CT ACC	ermer see	TRAN	SLATIO
					, C U.V.	IZIVA I	TOME	EN	·	DATE		COUNTRY		CLASS	SUBCLASS	YES	N
														•			
																	$\dashv$
	ОТТ	IER		AR	T (In	cludir	107 A1	thor	Title	Duta P	etinon	t Pages, Etc					
						-				Date, 1		t rages, Ett			<del></del>		
														<del></del>	<u>.</u>		
												·					
												<del>-</del>			<del></del> -		
																<del></del>	
										<del></del>							
							•	<del></del>			<del></del>						
EX	AMINER							DA	TE CO	NSIDERE	)						
			:					<u> </u>				<del></del>					
EX	AMINER	ci	tation	if no	erenc ot in	e confo	sider rmun	ed, w ice un	hethe d not	r or not e consider	itation ed. Inc	is in confo clude copy	rmance w of this for	ith MPEP rm with n	9 609; Draw l ext communic	ine thros cation to	ngh
		25	ntien	nf													

LIST DE		'EN	CB A	AND	(Modif	BLIC	CATIO	ONS FOR	ATTY. DOCKET NO. 479.	.58-3	SERIAL NO.		
APPLIO	<b>CFW</b> A	B I	NFO:	RMA	TIO ENT	N D	ISCL	OSURE	APPLICANT NAPOLEONE F	ERRARA, et al	0/360,235		
JAN 14	(Use	seve	ral si	heets	if n	ecess	агу)		FILING DATE June 1, 1	989	GROUP 186	·	
REMERENCE DE	PACES	ION	u.s.	. PAT	ENT D	OCUME	NTS						
EXAMINER .		l										FILING	DATE
INITIAL				DOCU	MENT	CUMBER		DATE	NAME	CLASS	SUBCLASS	IF APPR	
	_ <u> </u>	-	<u> </u>		₩-		$\vdash$						
	В	<u> </u>			<del> </del>	<u> </u>							
	С												
							FORI	EIGN PAI	ENT DOCUMENTS				
	İ			MC =	MENT N	a secto						TRANSL	ATION
							· 	DATE	COUNTRY	CLASS	SUBCLASS	YES	MC
	D				ļ	L			٠,				
	E				$oldsymbol{ol}}}}}}}}}}}}}}}}}}$								
	F												
	G												
	H								,			,	
OTI	HER					Al E	RT (:	Includir	ng Author, Tit	le, Date	, Pertin	ent Pa	ges
	J	-1	G. Be	eck (	et al. J. Leu	, "Is kocyt	olation e Bio.	n and Charac Vol. 42:5 (	terization of a Vascula 1987), p. 568.	r Permeabilit	y Factor from	Stimulated	u937
	ĸ	2	J.N. inhil	Bruc bitio	ce et on by	al., dexam	"Vascul ethasor	lar Permeabil ne <sup>m</sup> , J. Neuro	lity induced by protein osurg., Vol. 67 (1987),	product of m	alignant brain	n tumors:	
	L	3	G.R. facto	Cris	scuolo J. Ne	et a	l., "Fu	urther charac ol. 69 (1988)	eterization of malignant 1. pp. 254-262.	: glioma-deriv	ved vascular p		<u> </u>
	H	4	G. Go	ospoc uced	darowi by pi	cz et tuita	al., ' ry-deri	'Isolation ar ived follicul	nd characterization of a to stellate cells",	vascular end	othelial cell	mitogen	
		[							, Vol. 86 (1989), pp. 7				
		5	j. Pi	l or set	- 10		I cal at i	ion and abase	ncterization of a newly ol. 8:12 (1989), pp. 380		ndothelial cel	lmitogen	
			• :	· .			<u>.                                    </u>	·					
KANINER			dir.				DATE O	CONSIDERED					

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

### COPY OF PAPERS

1	E,	ζ.								ORIGINALLY FILE	D			
		<u> </u>	,				1_				—)			
Listy	γ↓ <sup>™</sup> FPA	FOR TES	PTO-	1449 AND	(Modi	fied) BLI	CAT	ION	8 FOR	ATTY. DOCKET NO. 479.	58-3	SERIAL NO. 0/360.235		
ATEN	CAN		STA	\TE	ŒN:	C			BURE	APPLICANT NAPOLEONE FI	ERRARA, et al	· · · · · · · · · · · · · · · · · · ·		
	(Us	e sev	eral :	sheet	s if	neces	sery)			FILING DATE June 1, 19	289	GROUP 186		
REFERENCE (	ESIGNA	TION	<u>U.S</u>	, PAT	TENT (	DOCUM	ENTS							
EXAMINER INITIAL	ļ ·	_	<del></del>	DOCU	MENT	MUMBE	R	<del>/</del>	DATE	NAME	CLASS	SUBCLASS	FILING IF APPR	
	-	╁	1—	┼	┼	┼-	┼	<del> </del>						
	В	+-	+-	-	╁	┼-	┼	┼	<u> </u>					
<del></del>	<u> </u>			<u> </u>		<u> </u>	<u> </u>	<u> </u>	<u> </u>					
<del> </del>		1	_			<del>,</del>	FO	REI	GN PAT	ENT DOCUMENTS				
				DOCU	MENT	MUNBE	<b>.</b>		DATE	,			TRANSL	ATION
	<del> </del>	┼—		1		T	<u>-</u>		- LAIE	COUNTRY	CLASS	SUBCLASS	YES	MC
•	D	┼	-	<del> </del>	-	-	-	<u> </u>		٠.				
	E	+	-	-	-	-	<u> </u>	<u> </u>	-					
-	F	┼	_	-		├	<del> </del>	_						
	<u>6</u>	-	<del> </del>	<del> </del>	├	├		-		<del></del>				<u> </u>
	<u>  H</u>		1	<u> </u>	L	<u> </u>		L		·	Щ			<u> </u>
OT	HER					A	RT tc.	(In	cludin	g Author, Titl	e, Date	, Pertin	ent Pa	ges
		6	G. C	Conn	et al				2 0 0 0 0 0					
	J	<u> </u>	der	ived	cell.	l ine#	Pro	c. Na	t. Acad. S	coprotein vascular endot ci. USA, Vol. 87 (1990)	thelial cell pp. 1323-13	mitogen from 27.	a rat glio	)M2-
	<del>                                     </del>	<del> </del>	_		-			,						
	K	7	G. C	Conn, telet	*Amid	no ac	id and	d cON/	sequence	s of a vascular endothel Nat. Acad. Sci., Vol. 8	ial cell mit	ogen that is	homo l ogous	3 to
						1.5			,	Hat. Acad. Scr., Vol. 8	7 (1990), pp	. 2628-2632.		
	L	8	D.R.	. Sen	ger e	t al.	, «Pui	rifice	tion of N	H <sub>2</sub> -Terminal Amino Acid S	or iones of C	wine Die Ver		
					-						requerice or u	umea rigitus	or-secrete	.ca
	<del>  _</del> _									p. 1774-1778.				
•	×	9	N. F Vol.	errar 47	ra et (1991)	al., ), pp.	"The . 211	Vascu -218.	ılar Endot	helial Growth Factor Fam	ily of Polyp	eptides', <u>J.</u>	Cell Bioch	iem.,
						111			:- :-					
	W	10	C. d Scie	le Vri	ies et Vol.	al. 255 (	"The	fos-	Like Tyro 989-991.	sine Kinase, a Receptor	for Vascular	Endothelial	Growth Fac	tor",
			pp.	989-9	<del>291.</del>		. *: -			,				
KAMINER							DATE		SIDERED		•			
					11.00	P. 1	,,,,		1463					

conformance and not considered. Include copy of this form with next communication to applicant.



### OniciNALLY FILED

																_						
				υ.	c.	8	39-	0.	53	- 3												
	F	OR	M P	то	-14	149	(Mc	odil	led	)					ATTY, DOCK	CET N	10		ERIAL			-
	1	UST	OF	P	ATI	EM	rs /	W	) P	UB	LIC	NOITA	SF	OR	479.58-3		.0.		60,			
		AP	PUC	:AN	IT;	5 11	NFC STA	H.	MI	1OF	1 D	ISCLO	SU	RE	APPLICANT				• • • •			-
		4	(I	Jsa	86						œ	rasary)			NAPOLEONE	F	ERRAI	RA	ET A	L.		
												~321)			FILING DATE	:			ROUP			_
	RE	FEF	REN	CE	DE	SK	SN/	\T)	ON	_		U.S	PA	TENT	DOCUMENTS	198	1_0		1	86_		_
•	ĐAN	NER!	Τ		Γ	_		_		_		T			DOCOMEN13		,					
	MI	WL.	-		L		Q.					DATE			NAME		aus	s	28282		LING DATE PPROPRIAT	
-			\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\		4	4	5	6	Ľ	5.	0	6/2	6/	84	Dvorak		260	-   -	12R	+-	THORN	-
-			\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\			-	Н	_	┡	<u> </u>	-	<u> </u>	_	·						1		-
_			A				Н	_		Н			$\dashv$					$\perp$				
_			Æ					7		H	$\dashv$	·	$\dashv$			-				_		
_			₩.	-	1		$\Box$						7			$\dashv$		- -		├-	·	-
_		$\dashv$	AG	+	4	4	4	4	4	4	$\bot$		$\Box$			$\dashv$		+		<del> </del>		_
_		ᅱ	HA.	+	+	+	+	+	4	+	-		4			$\Box$				$\vdash$		-
_		7	N	+	+	7	+	+	+	+	+		╁			-4		$\perp$				•
		$\Box$	Ж	1	I	I	1	1	†	$\dagger$	+		╁	<del>-</del> -	<del></del>	$\dashv$		╁-				
	•									FC	)R	EIGN	PA	TEN	DOCUMENT	<u>-</u>		Т.				
	· ·	T		Γ							Τ		T		POCOMENT	<u> </u>						
			r		D	XXI	ÆNT	NU.	821	ì		DATE			COUNTRY		aus	SUBC	aus -		HOULY	
			N.	0	3	1	10	9	8	9	1	5/30,	9	0 B	russels	-+;	212N	يرا		YES"	Ю	
_		1	W	W	0	8	4/	0	-	<del></del>	-	/7/84			CT				/12			
		7	W				П	-	-		-	·	-	<u> </u>	<del></del>	- -	207G	7/0	00			
		A	0	7			Н	-	-		-					-						
		1	,	7	ᅥ		$\vdash$	ᅱ		Н	_					$\perp$						
	-	0	THI	-J FR										<u> </u>								
	_	_			_			-	(111	CIL	101	ng Au	ith —	or, Ti	tle, Date, Perl	llner	it Pag	jes,	Etc.)			
	- 1	AR	,	1	0	.W	10	Le	ur	ng ,		Scie	nc	<u>e</u> , 1	/ol. 246,	р <b>.</b>	1306	. (	Dec	omb.		
_			+	+		_															=1	
		AS	L	1	Ρ.	J	. 1	Кe	ck		e	t al	• .	Scie	nce, Vol.	24	6. n	1	300			
					(E	)ec	· cer	nb	er		1	198	۵١				<u> </u>	· -	309	<u>,                                     </u>		
			T	1	Ġ.	E.	I	e	mk		<u>'</u>	+ =	<u> </u>	· .								
		AT	+	+	_		_	_			_	- a.		<u> </u>	rnal of Ne	euro	osci	enc	<u>e, </u>	<b>′</b> 01.	4	
_				L	МО	•	1,	1	<u>.</u>	_7	5	(Jar	nu	ary	1984).							
ĽΧ	AMIN	ÆR											•	D.	TE CONSIDERE	D						
					_			_														

EXAMINER: Initial If reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



			#												
FORM	1 P	го-	144	18 (	Μœ	ifie	<b>1</b> )			ATTY, DOCK	CET NO	Т	SEDIA		
LIST	OF	PA	TE	MTS	S AJ	ND I	PUBL	JCATIO	NS FOR	479.58-			SERIA 360,2		).
APP	uc	ΑN	ı.2	S.	FOF TAT	EME	ΠΟΝ ENT	DISCL	OSURE	APPUCANT Napoleon					<del>-</del>
				_				C0334Ŋ	)	FILING DATE		T	GROUP	,	
REFER	ENG	CE (	DES	iG	NAT	ПОИ	!	U.	S. PATENT	DOCUMENTS	707		<u>-</u>	86	
DWINER		-									<del></del>				
NTW		4	_	<u></u>	VAEN	U KV	/BER	עם	TE	KWE	١,	ws	SEGU	؞۱.	FLING DATE FAPPROPRIATE
	<u></u>	+	+	+	+	4	1.1						-	<del>~ </del>	WTHUTHALE
	A8 AC	+	╁	+	+	+-	H						<del> </del>	+	
<del></del>	<del>~</del>	+	╁	+	+	┨—	$\vdash$						1	+	
	Æ	+	+	+	╁	+	╁┼	╅						1	<del></del>
	Æ	+	$\dagger$	†	+		-	+		<u> </u>				$\perp$	
	AG	I	1	†	1	H	+	1-						$\bot$	
$ \Gamma$	ж	L	Г	Γ	I		+	1					<b> </b> -	1	
	AL	L	L	L	L		1	1					<u> </u>	4_	
	N	L					$oxed{oxed}$							╂	
	W.	L	L	L	Ш	Ц	1							╁	
							FO	REIGN	PATEN	T DOCUMENT				Щ.	<del></del>
- 1									Τ	TT DOCUMENTS					<del></del>
- 1	-		RESEAUN THEMASSOO					DATE	1	COUNTRY :	aus		zuoez	TRA	HOULTEN
I AL	7	T	1	T		Т	-		<del></del>			_[`		YES	Ю
- N	-	╁	+	+	+	+	H		<del> </del>			Т			<del>                                     </del>
	+	+	+	4	4	1_	Ш				7	$\top$			<del> </del>
- 1	4	1	$\perp$	$\perp$	$\perp$	$\perp$					<del>                                     </del>	╁			<del> </del>
10							П				<del> </del>	╁			
AP.	Γ	Τ	Τ	Т	T	$\Box$	+		<del> </del>		<del>↓</del>	_			
OT	HF	R		_	DT	<u>''</u>			<u> </u>	····					
<del></del>	T	'n		_		/m	CIUC	ung A	uthor, Ti	lle, Date, Perti	lnent Pa	ge:	s, Etc.)	)	
AR.	L	L	N.	-	٠										,
	L	Ŀ	кe	se	ar	ch	Cc	mmun	icatio	iochemical	61, No	5.	2, p	. 8	1 (June
			D.	G	os	po	dar	owin	2. o+	al Bissh					
AS .			, -	<u> </u>		•			-, -,	al. <u>Bioche</u>	mistry	<u>',</u>	Vol.	86	p. 882
	Н	_			9)										_
AT	Ц	_ !	٠.	G	os	pod	dar	owic	z, et a	al. as subr	nitted	i e	arlie	r	to relata
"		Ţ	J	> -	P	a tı	ret	App	1. Ser	No. 07/3	46,169	,	filed	-Me	<del>ay-2</del> , 199
AMINER										· · · · · · · · · · · · · · · · · · ·					
•									DA	TE CONSIDERE	D		-		
IINER: I	niti	al l	f re	a fe	ren	co	∞n	sidara	d whath	er or not citation					
- 200									u, miletii	er or not citation mance and no	on le ie	~-	· 10		

of



		σ.	c.	8	9.	-0	53	- 3											
	FOR								-				1						
	LIST	OF	PAT	ΈN	TS	AA	ו חו	)   1 1   1   1	LIC	ATIO	NS	FOR	479.	DOCKE . 58 – 3			SERIA 360		- •
				J 1	ST	ATI	EM	ENT	4 ()	NSCL	.OSL	IRE	APPLIC						
,		(U	30 84	<b>8</b> Y8	reJ	#he	eots	H r	1000	ossar,	Y)				Fer	ra	ra et	a.	l.
													FILING June	1, 1	989		GROUI 186	•	
	EFER	ENC	F D	ESI	G٨	LAT	ION			U.	S. P	ATENT	DOCUMEN	TS					
	WINER MVL			α	α	VEX	T KUI	/BER		0	NTE.		KALVE			aus			FLIGORE
		<u> </u>	+	L	L	L	L	L									s succ	22	F APPROPRIATE
		<u> </u>	╁	-	-	╀	╀	_	L						$\dashv$			$\dashv$	
	$\dashv$	- <del>~</del>	+-	$\vdash$	┝	╂-	╀	H	_	_								$\dashv$	
		Æ	1		-	┢	-	Н	$\dashv$									1	
		NF.	$\sqcap$		-	-		Н	$\dashv$	<u>'</u>	_	<del></del>			- -			$\Box$	
·		AG .					Н	1	7										
	-	AH .	Ш	$\Box$				7	7		$\neg$		<del></del>	<del></del>	+-			- -	
		N	Ц	4	4	4	$\perp$	I					<del></del>					+-	<del></del>
		N K	4	+	4	4	4	4	1		$\Box$						<del> </del>	╁	
		<u>~  </u>			L				┸					-			1	+-	
		_						FC	R	EIGI	Y P	ATENT	DOCUM	ENTS					
	1	-	D	oan	ÆK	T HV	V82F	1		DUTE			COUNTRY		au	22	STROTES	TR	HOULTS
	A	+	Т	Т	Т	Т	Т	Т	┞		+					_	www	YE	CH
	1		+-	├	┞	╀	╀	╀	<u> </u>		1					$\neg$			1
	+-	-	-	<u> </u>	┞	╀-	L		L		$\perp$								<del> </del>
· <del></del>	<u>W</u>			Ц		L	L	Ш			1					$\dashv$			+
	1 10	$\perp$	Ц			L									<del></del>	+			<del> </del>
	N	$\perp$	Ш								1					$\dashv$			<del> </del>
	OT	HE	7		ΑF	₹Т	(in	ciu	dlı	ng A	uth	or, Tit	e, Date,	Pertin	ant D				
•	AR		N		L	in	σ.	e	Ł	a I	В	ioche	mistry	. Vo	1 8	age	es, Etc.	721	
-	<del> </del>	H		_	+														
	ıs	H	N	•	Ue	enc	٥,	e	<u> </u>	al.	, 1	Bioch	emistr	y Vo:	1. 8	4,	pg.	328	2
		Ц	()	De	CE	emb	eı	: ]	9	87)									
1	AT	Ц	S		Sh	in	nas	ak	i,	, e	t a	11.,	Biocher	nical	lan	d 1	Resear	- Ch	
			Co	OM	mu	ni	Ca	ti	01	ns,	Vo	1. 1	52, pg.	717	7, (	Apı	ril 29		1988)
EXAMI	NER			-	-								E CONSID						
EXAMINI	ER: I	nitia	u if	te!	lar	- An		~	-	doe-		<u> </u>	•						
MPEP 60 of this for	9; Dr m w	aw l	ine าคร	thr	יטו טנ	ıgh	i Cit	atio	on ion	if no	a, v t in	onion ∞nion	rornoto mance an	itation of not o	n is ir ∞nsi	o der	onforma ed. Incli	ide uce	with ∞ov
					~!!	****	util	val	iUl'	10	abb	iicant.						_	173



U.C. 89-053-3 FORM PTO-1449 (Modified) ATTY, DOCKET NO. SERIAL NO. LIST OF PATENTS AND PUBLICATIONS FOR 479.58-3 360,235 APPLICANT'S INFORMATION DISCLOSURE **APPLICANT** STATEMENT Napoleon Ferrara et al. (Use several sheets if necessary) FILING DATE GROUP June 1, 1989 REFERENCE DESIGNATION U.S. PATENT DOCUMENTS DWINER MIM DOCUMENT MANSER FLING DATE DATE aus 2242582 F APPROPRIATE M 88 AC. Ю Æ Æ AG Ж A N FOREIGN PATENT DOCUMENTS DOCUMENT HUMBER TRAVSLATION COUNTRY ausSYDORS YES ĸ Ш W Ю ĸ ART (Including Author, Title, Date, Pertinent Pages, Etc.) OTHER D. M. Robertson et al. Biochemical Biophysical Research AR Communications, Vol. 149, No. 2, pg. 744 (December 16, 1987). D.R. Senger, et al. Cancer Research, Vol. 46 p. 5629, **AS** (November 1986). D.T. Connolly, et al., J. Clinical Investigation, Vol. 84 AT p. 1470 (November 1989). EXAMINER DATE CONSIDERED

EXAMINER: Initial If reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



LIS	T OF	PAT	ENT	S A FOI	ND RM	PU	N D	ATION:	S FOR SURE	479.58-3	-T NO	SFRIA 360	L NO. , 235	5	_
			S	TA.	ΓEΝ	IEN	r			APPUCANT Napoleo	n Ferr	350 0		•	
		30 8	evous	M 6/	1001	is if	noce	asan)		FILING DATE	989	GROUP		·	_
REFE	RENC	E D	ESIG	NA	πο	N_		U.S.	PATENT	DOCUMENTS					_
KULNER NTVL		T	ART (Incl. D.T. Conn. Vol. 264, F. Ishikawa					DATE	7			<del></del>		PLING DATE	<del>-</del>
	M		$\square$		T	T	T			KWE	- au	280	25 F	APPROPRIATE	
	18	1		$\perp$	I	I			<del> </del>						<b>-</b>
	<u> </u>	╀	H	4	4	$\bot$	П								-
	Æ	+	╟	+	+	+	$\sqcup$						+		-
	#	t	$\vdash \vdash$	╁	╁	╀	Н								
	AG			+	+	1	H		+	<del></del>					
	Ж		$\Box$	I	I		1		<del>                                     </del>	<del></del>		<del>- </del> -	- -		
	<u> </u>	Н		L	$\perp$		$\Box$				+		-		
	W	$\vdash$	- -	<del> </del>	╁_	Ц	4					<del></del>	+-		
	<u> </u>	Ц		_	L_	Ц	丄		<u> </u>			1	1-		
_						_F	ORI	EIGN	PATENT	DOCUMENTS	;		<del>'</del>		
		(	COUNT	e TKE	W8	er.		CKTE		CV A CTV	1	T	TRAY	HOTAE	
-	_	_	<del></del>				$\perp$			COUNTRY	are	arsara	YES	I NO	
-	4	1	$\coprod$	_	$\perp$	$\perp$		_ 7			<del> </del>			<del>"</del>	
-1'	<u> </u>	$\perp$	Ш		_[_						<del> </del>	<del> </del>		-	
1	X		П	T	T	7	1			· · · · · · · · ·	<del> </del>				
	0	Τ	П	7	T	†	<u> </u>				<u> </u>				
A	•		$\sqcap$	†	†	†	$\vdash$								
	THE	 R	<u></u> _	<u></u>						<u>·</u>					
T		_			- (1	TICH	ווטנ	ig Aui	hor, Tit	le, Date, Pertir	nent Pag	jes, Etc.	)		
, AR		1	).T	. (	Co	nne	11	<u>у,</u> е	t al.	, Journal c	of Bio	logica	1 0		
	- -		<del></del>			<u>.                                    </u>	11 -2	4 p	<u>· 20</u> 0.	L/ (1989).				_	
l s	Ш	F	. I s	h	ika	awa	,	et a	1., Na	ture. Vol	330			<del></del>	
										, ,,,,,	336	. 55 . 55	/ (P	pril	1989
AT	$\prod$	D	.R.	S	er	ige	r e	et a	1., <u>s</u> c	ience, Vol	. 219	p. 98	3 (F	eb. 2	5, 19
INER	Ш								<del></del>		_			<del></del>	
inch					•				DA	TE CONSIDERED					
									1						

EX MP MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



⊔st	OF	0-144 PATE!	NTS	ANI	D PI	JBLIC	2NOITA:	FOR	479.58-3		SERIAL 360	NO. , 235	
API	,UC	NTS	INFO	<b>JAN</b>	ITAN 13M	ON C	DISCLOS	JRE	APPLICANT				
	O.	10 BOY					ossary)		Napoleon	Ferra	ra, et	al.	
				_			———— ————		FIUNG DATE	1	GROUP 186		
REFER	IENC	E DES	3IGN	ATI	ON		U.S. I	PATENT	DOCUMENTS				
MINL			000A	4EXT	KUME	ER	DATE		KWE	aus	S SEGLE	FUIG S F APPRO	
	<u> </u>	44	+	1_	Ш							-	
	1.8 1.C	╁┼	+-	╀	H	_	<del> </del>					1	
	AD	++	╁	+	H	+	<del> </del> -	-					
	Æ	††	十	H	$\vdash \vdash$	+-	<del> </del> ,	<del> </del>					
	Æ	$\prod$	T	П	H	$\top$	<del>                                     </del>	+		-			
]	AG	П	$oldsymbol{\Box}$	口						<del></del>	<del>- </del> -	┨	
	HA.	-	44	Ц	$\perp$	$\perp$						<del>                                     </del>	
	N	┼┼	┦┤	$\dashv$	+	+		<u> </u>					
$\neg +$	<del>~</del>	╁┼	╁┤	$\dashv$	- -	╁┤		<u> </u>		_			
						<u> </u>						<u></u>	
Т						-07	IEIGN I	AIEN	T DOCUMENT	s			
		Ø	ĊWEH	IT, HVI	VBER		CATE		COUNTRY	aus	SYDOYS	TRANSLATI	ON
1	AL I	<del></del>							YES I	<u>0</u>			
_	NI I	$\dashv\dashv$	+	╁	╂┈	╟							
	W	╂╂	┰	╀	H						<u> </u>		
	-	+	+	╀	┦┦					1.			
	0	44	4	$\perp$	Ш								
	P	Щ	丄	L	Ш	┸							_
0	THE	R	_ A	RT	(In	clud	ing Au	hor, T	ltle, Date, Pert	Inent Pa	ges, Etc.	<u></u> )	<del>-</del>
,,	, L	J							oc. Natl.				 ''-
<u> </u>	1	g	. 8	02		(Fe	bruar	y 198	19).		, 0		<u>,</u> vo.
	.										<del></del>		_
100											<del></del>		
145	+	<del>                                     </del>											_
_  ^\		<del> </del>											_
AT	·  -					·						-	
TA	$\perp$	<u> </u>								.~			
- -	$\perp$	!						'	ATE CONSIDERE	:0			

(Information Disclosure Statement—Section 9 PTO-1449 (Modified) [6-1]—page 6 of 6